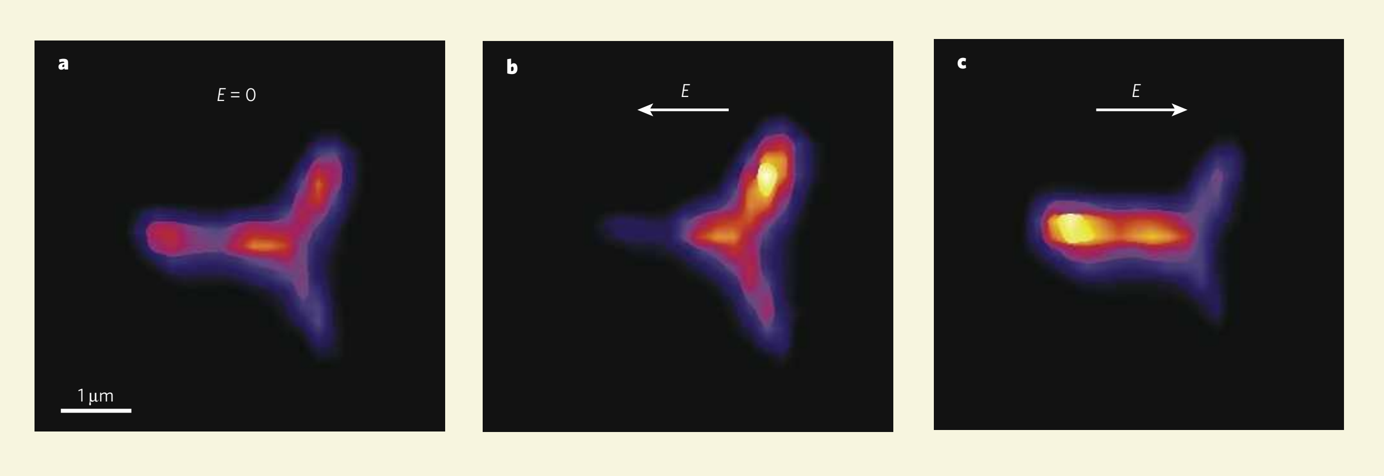

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Figure 1 | **Enhanced fluorescence in a nanowire tripod.** Nanowires made of semiconductors fluoresce. Kuno and colleagues[5] have made branched structures that contain nanowires, such as this tripod made from the semiconductor cadmium selenide. **a**, This image shows the baseline fluorescence of the tripod in the absence of an electric field. **b**,**c**, When an external electric field is applied, enhanced fluorescence occurs in regions of the tripod that are closest to the positive electrode; fluorescence is diminished at the opposite side. The authors suggest that mobile charge carriers in the semiconductor cause this effect.

charge that presumably causes the enhanced fluorescence, thereby quenching it.

With their working hypothesis in mind, Kuno and colleagues[5] went on to study the effect of electric fields on the motion of nanowire bundles floating in solvents. The authors found not only that the bundles rotated into alignment with the applied fields, but also that their centres of mass moved towards either one of the electrodes. This behaviour can be explained only if mobile charges are present in the nanowires, rather than static dipoles — in agreement with the authors' theory. Furthermore, the authors were able to estimate the net surface charge per nanowire by modelling the various factors associated with the movement, such as torques, rotational speeds and solvent viscosities. They also showed that, surprisingly, the sign of the net charge changes depending on the solvent: the nanowires accumulated excess negative charge in some solvents, but positive charge in others.

Kuno and colleagues' work might provide fresh insight into a long-standing question about semiconductor nanoparticles: why does the fluorescence of CdSe quantum dots blink on and off[3]? The model usually invoked to explain such blinking relies on the idea of electron–hole pairs. It is useful to imagine that, when an electron in a semiconductor is promoted to an excited state by a photon, a positively charged 'hole' also forms, which behaves like a mobile charge carrier. In a 'switched-on' quantum dot, fluorescence occurs efficiently when electrons and holes recombine. But sometimes an electron (or a hole) can become trapped on or near the surface of the dot[7,8]. The corresponding hole (or electron) in the core of the dot can then lose energy in a rapid non-radiative pathway that competes with fluorescence, so that the dot 'switches off' and becomes dark. The charge carrier on the surface can eventually return to the core, restoring the natural uncharged state, and thus the on–off cycle of fluorescence can repeat itself extensively.

Tantalizing support for this model has been provided by sensitive experiments[9] showing that the charge on quantum dots 'blinks' on and off in a way that is clearly analogous to the observed intermittent fluorescence. But it has proven surprisingly difficult to link these two phenomena unambiguously. By providing direct evidence for the correlation between electric field, fluorescence and the net accumulation of surface charge on nanoparticles, Kuno and colleagues' results[5] might provide a crucial step towards explaining the root causes of these mysterious blinking phenomena. ■

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NEUROSCIENCE

Neighbourly synapses

Bernardo L. Sabatini

Experiences shape our behaviour, memories and perception. Mechanistically, they also influence the brain's circuitry, and cooperativity between neuronal contacts during learning may contribute to this process.

Neuronal plasticity describes experience-related and development-associated structural and functional changes in the brain, which contribute to, among other processes, memory formation. Such changes occur at many levels; for example, depriving an animal of visual stimuli results in both small-scale modifications in neuronal receptors, and large-scale rewiring of neural circuits[1,2]. Many of these changes involve plasticity at the level of synapses, the specialized contact points between neurons, and much of the tremendous learning power of the mammalian brain is thought to arise directly from the vast number of synapses that it contains. So understanding the degree to which each synapse can be independently regulated is necessary to comprehend the computational capacity of our brains. Harvey and Svoboda[3] (page 1195 of this issue) carried out micrometre-scale analysis to determine whether the induction of an activity-dependent form of synaptic plasticity, known as long-term potentiation (LTP), at one synapse alters the properties of its immediate neighbours.

Neurons communicate with each other through neurotransmitters. A stimulated neuron (the presynaptic neuron) fires an action potential, which results in the release of neurotransmitters from its axon into the synaptic cleft between it and another neuron (the postsynaptic neuron). Released neurotransmitters bind to receptors on the postsynaptic neuron

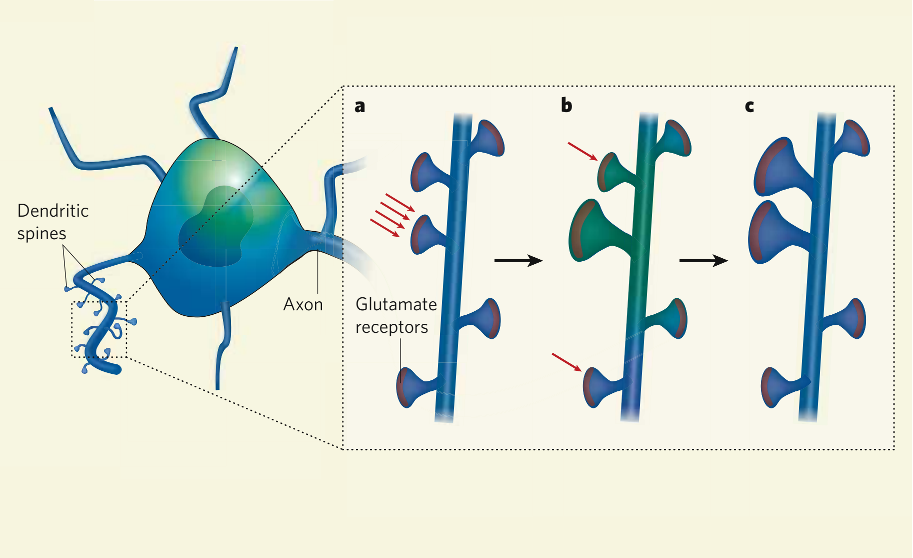

Figure 1 | Cooperativity between synapses. Five dendritic spines, each containing the same number of postsynaptic glutamate receptors, are shown. **a**, When a strong stimulus (red arrows) induces long-term potentiation (LTP) at a single spine, it causes the stimulated spine to grow (**b**). Harvey and Svoboda[3] find that LTP induction at one spine also lowers the threshold for LTP induction at its immediate neighbours (within a distance of 10 micrometres). Consequently, weak stimulation of a nearby spine (red arrow) is sufficient to induce LTP and functional and structural plasticity in the neighbouring synapses (**c**). Weak stimulation of the lower spine that lies outside this zone, however, does not induce plasticity. Approximately 10 minutes after the original stimulation, the plasticity threshold returns to normal and spine growth is stabilized.

and allow ion entry. Excitatory synapses are often made onto dendritic spines (small projections along dendrites) on the postsynaptic neuron. LTP describes strengthening of synaptic communication between two neurons, observed when they are persistently activated simultaneously.

Studying synapses in the hippocampus of the mouse brain, Harvey and Svoboda focused on the effects of LTP on synapses that are located close to the potentiated synapse but that are not stimulated directly. Similar work has been done previously, but the earlier findings[4–6] have been controversial because, depending on sample preparation and the protocol for LTP induction, synapses were reported to be depressed, unaffected or potentiated.

The problem with most previous studies on the effects of LTP on unstimulated synapses is that the experimenter did not choose which synapses to study, and instead analysed those that happened to be stimulated by an electrode. Axons in the hippocampus are divergent and meandering, so even weak stimuli delivered through an electrode placed close to the cell of interest stimulate synapses dispersed throughout large sections of the dendritic arbour. Consequently, the spatial arrangement and the number of actively communicating synapses remain unknown, making it difficult to probe the independence of synaptic plasticity at a fine scale.

But technological advances allow delivery of stimuli to postsynaptic termini in various spatio-temporal patterns. The trick is to bypass the presynaptic terminal and use light to trigger a chemical reaction that produces the neurotransmitter glutamate and directly stimulates the dendritic spine. Addition of a large, light-absorbing side group to glutamate makes it inactive, or what is known as caged; light pulses can be used to rapidly break down the cage, releasing the active neurotransmitter. For example, two-photon excitation is used to trigger glutamate uncaging and release in sub-femtolitre (less than 10^{-15} litres) extracellular volumes. Thus, glutamate is delivered to individual spines located relatively deep within the brain tissue, under conditions that mimic the time course of synaptically released glutamate.

This approach was previously used[4] to study synaptic plasticity in slices of brain tissue maintained in culture and led to the discovery that LTP induction at a single postsynaptic terminus is accompanied by stable growth of the stimulated spine. The structural and functional plasticities were limited to the stimulated spine, indicating that both types of plasticity are synapse-specific.

Harvey and Svoboda[3] asked whether LTP induction at one spine might alter the ability of neighbouring spines to undergo plasticity. They find that, after LTP induction, although structural and functional plasticity is limited to the stimulated spine, surprisingly, the threshold for the induction of plasticity in its immediate neighbour synapses is dramatically reduced. This effect is seen in spines located within roughly 10 micrometres of the stimulated spine and lasts for about 5 minutes (Fig. 1). Furthermore, the phenomenon is robust, because it occurred not only in glutamate-uncaging experiments but also in response to electrical induction of LTP, which is more similar to the physiological setting.

The mechanism underlying the reduced threshold for plasticity in neighbouring synapses is unknown. It could be simple, with LTP induction at one spine activating a pathway that enhances synaptically evoked calcium influx into neighbouring spines; alternatively, it may involve more complex adjustments of the LTP-induction machinery. But one point is certain — spatially clustered groups of synapses act in a mutually reinforcing and cooperative way.

These results[3] may also help to explain the findings of a previous study[5], which showed that potentiation triggered by strong synaptic stimulation spreads to non-stimulated synapses. In hindsight, instead of potentiation spreading, it is probable that the threshold for the induction of plasticity in the adjacent synapses was lowered; consequently, subthreshold stimulation, which is normally used to probe the state of neighbouring synapses, was enough to induce LTP, giving the impression that potentiation had spread.

Harvey and Svoboda's findings open several avenues of research. Computational and theoretical neuroscientists will probably find that lowering of the LTP threshold at neighbouring synapses, in response to LTP of one synapse, endows neural networks with new behavioural and learning capabilities[7]. Cell biologists will be fascinated by the mechanisms underlying the 'priming' of neighbouring synapses for LTP induction. For example, they would want to know what molecules are released from the potentiated spine and what pathways they activate on arrival at the neighbouring spines. Electrophysiologists would want to know whether the spatial and temporal spread of the effect on the LTP threshold depends on the number of synapses potentiated. Furthermore, they would be curious to establish how the effects described by Harvey and Svoboda relate to synaptic capture and tagging. (These are mechanistically distinct phenomena that occur over long timescales and in response to strong stimulation of many synapses, and allow the potentiation of one set of synapses to alter the threshold for plasticity induction at others.)

Returning to the question of the organizational scale of regulation in the brain, these findings[3] indicate that synapses located close to each other are neighbourly, acting, to some extent, as a cooperative unit. Co-activation of neighbouring synapses on a single dendritic segment is known to trigger local action potentials that act as spatially delimited, associative signals for the induction of LTP[8]. Owing to these mechanisms, synapses that tend to fire together and that are near each other on a dendrite will be potentiated more readily than simultaneously active synapses separated by large distances. If potentiation increases the likelihood that a synapse is preserved during development, this may lead to

TECHNOLOGY

The art of illumination

In November 2006, the Yamaguchi Prefectural Art Museum in southern Japan held an exhibition entitled 'The Trip to Sesshu'. It commemorated the 500th anniversary of the death of the Zen Buddhist monk and painter Sesshu Toyo, whose delicate *suibokuga* ink paintings have been designated 'National Treasures' by the Japanese government.

So that visitors could appreciate Sesshu's scrolls as closely as possible to the way original admirers did — under candlelight or torchlight — some of the paintings were illuminated by a specially designed light-emitting diode (LED) system. Tsunemasa Taguchi and Michitaka Kono now provide the technical details of that system (T. Taguchi and M. Kono *J. Light Visual Environ.* **31,** 149–151; 2007).

LEDs are solid-state light emitters known for their energy efficiency, flexibility of design and robustness. For a long time, they were made to emit light only in a particular part of the visible-wavelength spectrum. But in the mid-1990s a new generation emerged, based on blue LEDs covered with a yellow phosphorescent layer, which emitted bright, white light.

Taguchi and Kono's lighting system used special LEDs that contained three different phosphors, each emitting at different frequencies. This meant that the white light emitted had a particularly high colour quality, as quantified on a scale known as the colour-rendering index. To optimize viewers' appreciation, the authors tailored the LEDs to render the earthy red colours characteristic of the antique scrolls especially well.

T. TAGUCHI & M. KONO

The individual lights were positioned so as to distribute light evenly on the artwork (first two paintings pictured), rather than scattering it around them as fluorescent lamps would do (paintings in background). The output of the LEDs was stable and did not cause heating, thus assisting preservation of the precious scripts.

White LEDs are becoming ever brighter, more efficient and less expensive. As a result, traditional light bulbs are increasingly on the way out. Large-scale applications, such as car lights, traffic signals and Christmas decorations, are where the economic benefits of LED use are being felt. But the illumination of antique Japanese art must surely rank as one of the diodes' most aesthetically pleasing applications.

Liesbeth Venema

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the spatial clustering of synapses with similar firing patterns. Thus, for some forms of activity-dependent plasticity in the hippocampus, the fundamental unit of regulation might be larger than an individual synapse[9], and rather a physically clustered cohort of synapses with similar firing patterns, whose spatial arrangement on dendrites arises naturally following mutually reinforcing interactions between synapses.

It is neuroscientists' goal to understand the plastic features of the brain that make storing memories and learning new behaviours possible. In trying to achieve this formidable goal, many neuroscientists hope that, by uncovering the mechanisms behind the regulation of individual synapses, they will reveal the rules that govern the wiring of the brain. Harvey and Svoboda's results introduce a new level of complexity. They demonstrate that these rules vary across distances as short as a few micrometres, and are themselves altered on a minute-by-minute time frame. ■

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METROLOGY

New generation of combs

Steven T. Cundiff

To measure an optical frequency, you are best off using an optical frequency comb. A radical approach shakes up how these combs are produced, and will permit their closer integration into optical-fibre technology.

Increasing the range over which frequencies can be accurately measured is an exertion driven both by applications (making sure that a mobile phone uses the right channel, for instance) and by fundamental physics: time and frequency are the most accurately measured physical quantities, and thus are often used in tests of theories such as relativity and quantum mechanics. Optical frequency combs[1,2] — arrays of regularly spaced, well-defined reference frequencies — have revolutionized these endeavours[3,4]. Optical atomic clocks using this form of benchmarking can be more precise[5] than the very best clocks referenced to the current caesium atomic time standard, and combs are increasingly being used for sensitive and rapid detection of molecular processes[6]. The growing importance of the technique was recognized by its appearance in the citation for the 2005 Nobel Prize in Physics[7].

On page 1214 of this issue, Del'Haye *et al.*[8] describe the creation of an optical frequency comb using a toroidal glass microresonator. The very strong light fields produced drive the optical response of the glass into the nonlinear regime, where the principle of wave superposition no longer applies and waves can mix with one another to create new frequencies. The flexibility and small size of this apparatus give it huge potential for use in diverse areas, from telecommunications to astrophysics.

Frequency combs provide a way of accurately measuring frequencies that are too high to be measured directly. At radio frequencies, combs are produced by driving an electrical element, typically a step-recovery diode, with a simple, sinusoidal input signal. Once this sine wave exceeds a threshold, the diode converts it into a square wave, which contains new frequencies. The highest frequency is determined by the switching time, and is around 100 picoseconds for the best diodes. The standardized comb frequencies thus generated are integer multiples (harmonics) of the well-known input-wave frequency.

Generating a comb with a useful frequency spacing at optical frequencies requires a different approach. Until a few years ago, this meant injecting light from a continuous-wave laser into an optical cavity containing an electro-optic modulator driven by a radio-frequency signal[9]. The result was a cascade of evenly spaced frequency lines above and below the laser's optical frequency, corresponding to adding or subtracting integer multiples of the radio-frequency modulator signal, with each line generating the next. Combs generated in this way generally spanned a frequency range of several terahertz.